

=> d que stat 179

L78 1 SEA FILE=REGISTRY ABB=ON 76555-98-1/RN

L79 7 SEA FILE=HCAPLUS ABB=ON L78

=> d ibib abs hitstr 179 1-7

L79 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:748108 HCAPLUS

DOCUMENT NUMBER: 135:300482

TITLE: Isolation of functionally active γ -secretase presenilin 1 complex and fluorescence assay for γ -secretase activity and inhibitors

INVENTOR(S): Roberts, Susan B.; Hendrick, Joseph P.; Vinitzky, Alexander; Lewis, Martin; Smith, David W.; Pak, Roger

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001075435	A2	20011011	WO 2001-US10453	20010330
WO 2001075435	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GU, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2405332	AA	20011011	CA 2001-2405332	20010330
US 2002025540	A1	20020228	US 2001-823153	20010330
US 6713248	B2	20040330		
EP 1305634	A2	20030502	EP 2001-922976	20010330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004505608	T2	20040226	JP 2001-572863	20010330
US 2004121411	A1	20040624	US 2003-713981	20031114
PRIORITY APPLN. INFO.:				
			US 2000-194495P	P 20000403
			US 2001-823153	A3 20010330
			WO 2001-US10453	W 20010330

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ -secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ -secretase. In one embodiment, the isolated γ -secretase protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β -amyloid precursor protein (β APP) by γ -secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ -cleaved β APP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ -cleaved β APP fragment, with substantially no cross-reactivity to uncleaved β APP or to other types of γ -cleaved β APP fragments, while a second fluorescent adduct binds to a portion within the

amino-terminal region on the γ -cleaved β APP fragment.
Detection of binding to the γ -cleaved β APP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

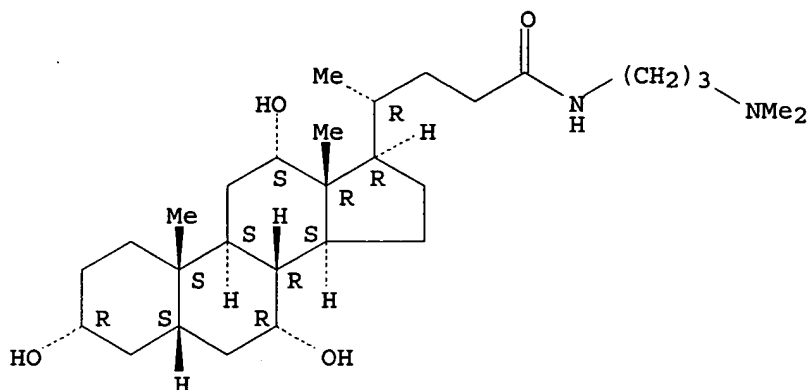
IT 76555-98-1

RL: NUU (Other use, unclassified); USES (Uses)
(solubilizer; isolation of functionally active γ -secretase presenilin 1 complex and fluorescence assay for γ -secretase activity and inhibitors)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:75714 HCAPLUS

DOCUMENT NUMBER: 108:75714

TITLE: Steroids and their cyclic hydrocarbon analogs with amino-containing sidechains, useful as antidiabetic agents and inhibitors of phospholipase A2

INVENTOR(S): Johnson, Roy A.; Bundy, Gordon L.; Youngdale, Gilbert A.; Morton, Douglas R.

PATENT ASSIGNEE(S): Upjohn Co., USA

SOURCE: PCT Int. Appl., 177 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

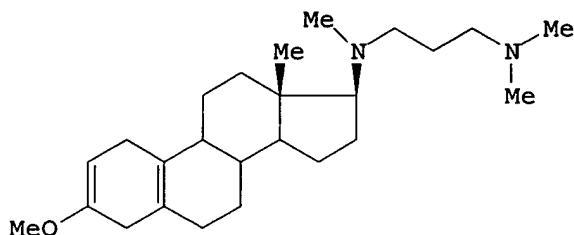
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8702367	A2	19870423	WO 1986-US2116	19861007
WO 8702367	A3	19880630		
W: JP, US, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
EP 243449	A1	19871104	EP 1986-906569	19861007
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63501217	T2	19880512	JP 1986-505710	19861007
US 4917826	A	19900417	US 1987-117851	19870616
US 5196542	A	19930323	US 1991-657721	19910220
US 5145874	A	19920908	US 1991-663037	19910225
US 5187299	A	19930216	US 1991-793486	19911113

US 5274089	A	19931228	US 1992-972693	19921106
US 5334712	A	19940802	US 1992-976751	19921116
US 5373095	A	19941213	US 1993-126153	19930923
US 5621123	A	19970415	US 1994-247169	19940520
PRIORITY APPLN. INFO.:			US 1985-788995	A2 19851018
			US 1986-843120	A2 19860324
			WO 1986-US2116	W 19861007
			US 1987-117851	A3 19870616
			US 1989-394396	A3 19890815
			US 1991-657721	A3 19910220
			US 1991-657729	B1 19910220
			US 1991-793486	A3 19911113
			US 1992-972693	A3 19921106
			US 1992-976751	A3 19921116

OTHER SOURCE(S): CASREACT 108:75714
GI



AB A wide variety of steroids and nonsteroidal analogs bearing amino-containing sidechains were prepared for use as antidiabetic agents and in the treatment or prevention of phospholipase A2-mediated conditions. Reductive amination of estrone Me ether with $\text{Me}_2\text{N}(\text{CH}_2)_3\text{NH}_2$ and HCO_2H at $160-170^\circ$ gave N-[3-(dimethylamino)propyl]-N-formyl-3-methoxyestra-1,3,5(10)-trien-17 β -amine, which was reduced by LiAlH_4 in dioxane to the N-Me derivative. This underwent Birch reduction, followed by 3 recrystns.

in

Et₂O-MeCN, to give estradienamine derivative I. In the perfused guinea pig lung, I completely inhibited phospholipase A2 at 4×10^{-7} M.

IT 76555-98-1P

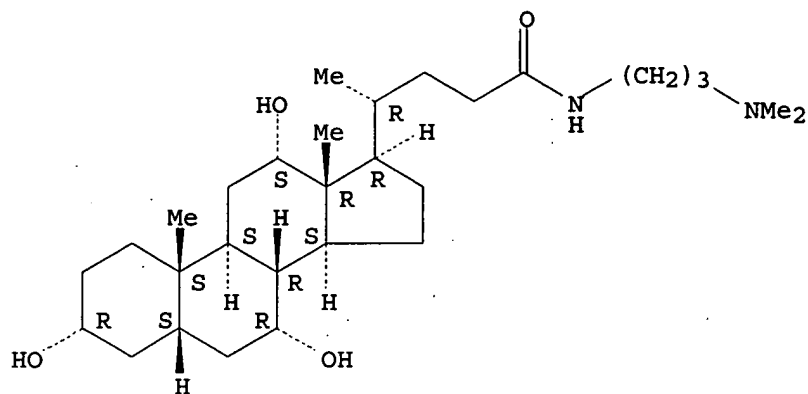
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in synthesis of phospholipase A2-inhibiting amino steroids and analogs)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:187118 HCAPLUS

DOCUMENT NUMBER: 104:187118

TITLE: Fixed steroids

INVENTOR(S): Itagaki, Koji; Ito, Takeshi; Ando, Kyoto

PATENT ASSIGNEE(S): Mitsubishi Chemical Industries Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60133005	A2	19850716	JP 1983-241342	19831221
PRIORITY APPLN. INFO.:			JP 1983-241342	19831221

AB Products useful as carriers in affinity chromatog. are prepared by amidation of carboxylated steroids with polyalkylenepolyamines and reaction of the amides with insol. matrix polymers having amine-reactive groups. Thus, heating 20 g Et cholate with 100 g Me₂N(CH₂)₃NH₂ 16 h at 140° gave 21.1 g amide. Heating 19.4 g amide and 5 g chloromethylated styrene-divinylbenzene polymer in 1:1 dioxane-MeOH for 16 h at 70° gave 10.3 g fixed steroid (ion exchange volume 1.08 mequiv/g dry resin).

IT 76555-98-1D, reaction products with chloromethylated styrene copolymers

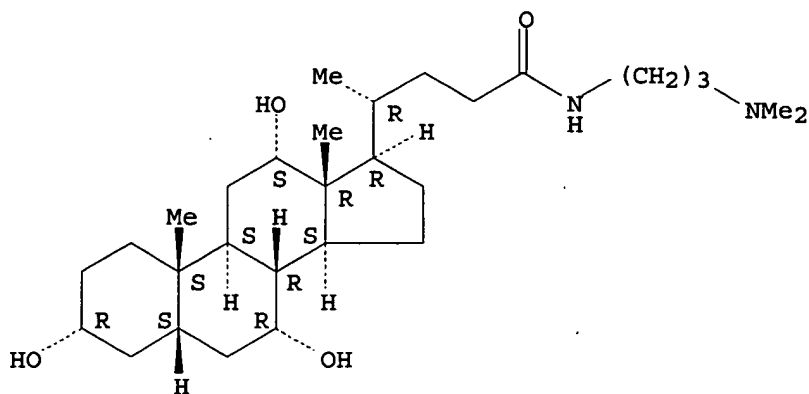
RL: USES (Uses)

(carriers in affinity chromatog.)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:402687 HCAPLUS

DOCUMENT NUMBER: 99:2687

TITLE: Sulfobetaine derivatives of bile acids: nondenaturing surfactants for membrane biochemistry

AUTHOR(S): Hjelmeland, Leonard M.; Nebert, Daniel W.; Osborne, James C., Jr.

CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA

SOURCE: Analytical Biochemistry (1983), 130(1), 72-82
CODEN: ANBCA2; ISSN: 0003-2697

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The syntheses of 4 new sulfobetaine derivs. of bile salts are presented, along with a general set of criteria for useful detergents in membrane biochem. Phys. properties including the critical micelle concentration, aggregation

number, partial sp. volume, critical micellar temperature, UV-visible spectrum, and CD

spectrum were examined for the new compds. To examine the interaction of this class of compds. with macromols., CHAPS was further studied. CD spectra of apolipoprotein C-III2 were measured in the presence of varying concns. of CHAPS to determine the effect of this compound on secondary structure.

Gel-exclusion chromatog. and sedimentation equilibrium studies of cytochrome P 450 in the presence of CHAPS was also performed to establish the ability of this detergent to disaggregate cytochrome P 450 to a monomeric/dimeric state.

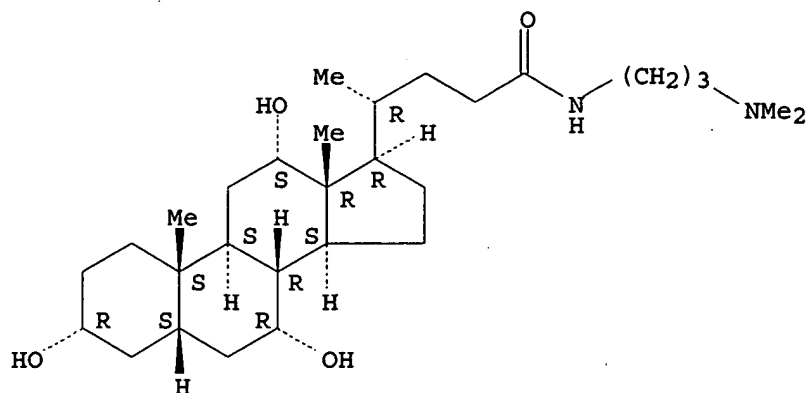
IT 76555-98-1P

RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent) (preparation and alkylation of)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1982:452173 HCAPLUS

DOCUMENT NUMBER: 97:52173

TITLE: Nondenaturing zwitterionic detergents for membrane biochemistry

INVENTOR(S) : Hjelmeland, Leonard

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: U. S. Pat. Appl., 47 pp. Avail. NTIS Order No.

PAT-APPL-6-294 203

CODEN: XAXXAV

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 294203	A0	19820409	US 1981-294203	19810819
US 4372888	A	19830208		
US 181465	A0	19810327	US 1980-181465	19800826
WO 8300694	A1	19830303	WO 1982-US1123	19820819
W: JP				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				
JP 58501279	T2	19830804	JP 1982-502842	19820819
EP 85717	A1	19830817	EP 1982-902934	19820819
EP 85717	B1	19861029		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
CA 1179326	A1	19841211	CA 1982-409779	19820819
AT 23166	E	19861115	AT 1982-902934	19820819
RITY APPLN. INFO.:			US 1980-181465	19800826
			US 1981-294203	A 19810819
			EP 1982-902934	A 19820819
			WO 1982-US1123	W 19820819

AB Preparation of 2 nondenaturing zwitterionic detergents, 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS) and 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), is described for solubilization of membrane proteins. CHAPSO was 2-fold more effective in solubilizing active opiate receptors than CHAPS.

IT 76555-98-1P

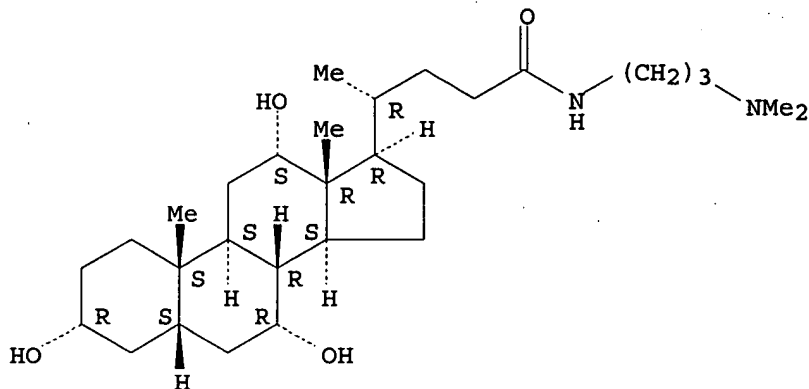
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reactions of, with propanesultone or sodium chlorohydroxypropanesulfonate)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:438693 HCAPLUS

DOCUMENT NUMBER: 95:38693

TITLE: Nondenaturing zwitterionic detergents for membrane biochemistry

INVENTOR(S): Hjelmeland, Leonard M.

PATENT ASSIGNEE(S): United States Dept. of Health, Education, and Welfare, USA

SOURCE: U. S. Pat. Appl., 22 pp. Avail. NTIS Order No. PAT-APPL-181 465.

CODEN: XAXXAV

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 181465	A0	19810327	US 1980-181465	19800826
CA 1173823	A1	19840904	CA 1981-382720	19810728
EP 46523	A1	19820303	EP 1981-106105	19810804
EP 46523	B1	19840725		
R: BE, CH, DE, FR, GB				
US 294203	A0	19820409	US 1981-294203	19810819
US 4372888	A	19830208		
JP 57073095	A2	19820507	JP 1981-132668	19810826
JP 03002877	B4	19910117		

PRIORITY APPLN. INFO.: US 1980-181465 A 19800826

AB Preparation of zwitterionic detergents, which are a combination of a bile salt hydrophobic group and a sulfobetaine-type polar group, is described for solubilizing membrane proteins in a nondenatured state. 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate (I) preparation is described. The Et₃NH⁺ salt of cholic acid was formed in THF, then ethylchloroformate was added to precipitate Et₃NHCl, which was removed from the mixed anhydride by filtration. The mixed anhydride reacted with

3-dimethylaminopropylamine to form N-(3-dimethylaminopropyl)cholamide (II), EtOH, and CO₂. In the final step, the tertiary amine group of II reacted with propane sultone to give the sulfobetaine, I. The yield was 75-80% theor., and the purity of I was >95% as judged by TLC.

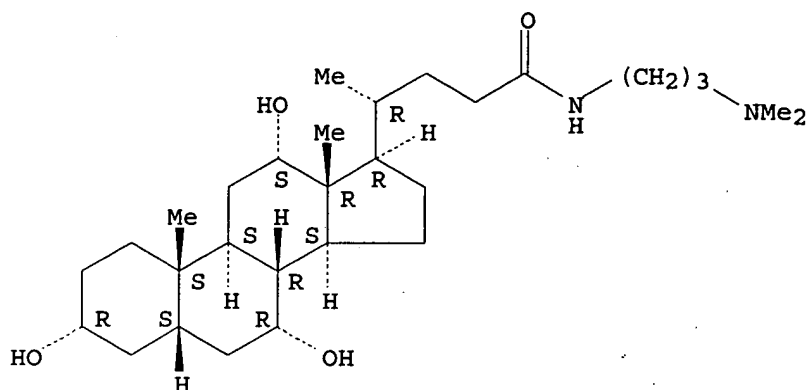
IT 76555-98-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with propanesultone)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L79 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:79812 HCAPLUS

DOCUMENT NUMBER: 94:79812

TITLE: A nondenaturing zwitterionic detergent for membrane biochemistry: Design and synthesis

AUTHOR(S): Hjelmeland, Leonard M.

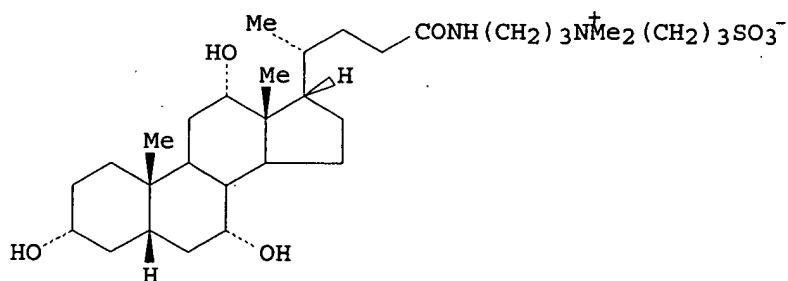
CORPORATE SOURCE: Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1980), 77(11), 6368-70
CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB The synthesis and evaluation of a new detergent that is a zwitterionic derivative (I) of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

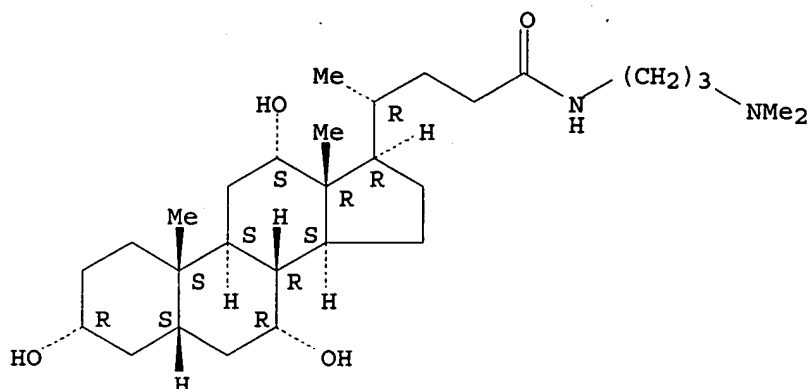
IT 76555-98-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with propanesultone)

RN 76555-98-1 HCAPLUS

CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Christopher
Nichols
10/7/3981

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

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SESSION

FULL ESTIMATED COST

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0.21

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DICTIONARY FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1

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*
* The CA roles and document type information have been removed from *
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* available and contains the CA role and document type information. *
*

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> e mchapso/cn 5

E1 1 MCH90/CN
E2 1 MCHA-1A4/CN
E3 0 --> MCHAPSO/CN
E4 1 MCHB PROTEIN (ESCHERICHIA COLI CFT073 STRAIN CFT073 GENE MCH B)/CN
E5 1 MCHC PROTEIN (ESCHERICHIA COLI CFT073 STRAIN CFT073 GENE MCH C)/CN

=> e "n-(3(dimethylamino)propyl)3,7,12-trihydroxy(3a, 5b, 7a, 12a)cholan-2-amide"/cn

E1 1 N-(3'-SULFOPHENYL)ANTHRANILIC ACID/CN
E2 1 N-(3'-TRIFLUOROMETHYL-6'-CARBOXYPHENYL)ANTHRANILIC ACID/CN
E3 0 --> N-(3(DIMETHYLAMINO)PROPYL)3,7,12-TRIHYDROXY(3A, 5B, 7A, 12A) CHOLAN-2-AMIDE/CN
E4 1 N-(3(R)-(4-CHLOROPHENYL)-1(S)-METHYL-2(S)-PHENYLBUTYL)-2-((3,5-DIFLUORO-4-METHYLPHENYL)OXY)-2-METHYLPROPANAMIDE/CN
E5 1 N-(3(S)-(4-CHLOROPHENYL)-1(S)-METHYL-2(S)-PHENYLBUTYL)-2-((3,5-DIFLUORO-4-METHYLPHENYL)OXY)-2-METHYLPROPANAMIDE/CN
E6 1 N-(3(TERT-BUTOXYCARBONYLAMINO)PROPYL)-1-DEOXYNOJIRIMYCIN/CN
E7 1 N-(3)-METHYL-N-(5)-ETHYL-N-(5)-MONOHYDROLUMIFLAVIN/CN
E8 1 N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE/CN
E9 1 N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE HYDROBROMIDE/CN
E10 1 N-(3,3,3-TRIFLUOROETHYL)NORAPOMORPHINE HYDROCHLORIDE/CN
E11 1 N-(3,3,3-TRIFLUOROPROPYL)-1H-INDAZOLE-5-CARBOXAMIDE/CN

Searched by: Mary Hale 571-272-2507 REM 1D86

E12 1 N-(3,3,3-TRIFLUOROPROPYL)-N-((2,3-DICHLOROPHENYL)METHYL)PIPERIDIN-4-AMINE FUMARATE/CN

=> s dimethylamino(1)propyl(1)trihydroxy(1)cholan(1)amide

462857 DIMETHYLAMINO
2149448 PROPYL
4 PROPYLS
2149448 PROPYL
(PROPYL OR PROPYLS)
73372 TRIHYDROXY
16504 CHOLAN
3410082 AMIDE
1031 AMIDES
3410082 AMIDE
(AMIDE OR AMIDES)

L1 4 DIMETHYLAMINO(L) PROPYL(L) TRIHYDROXY(L) CHOLAN(L) AMIDE

=> fil hcapl;s l1 or dimethylamino(1)propyl(1)trihydroxy(1)cholan(1)amide or mchapso

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.29	24.50

FILE 'HCAPLUS' ENTERED AT 13:57:42 ON 22 MAR 2005
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FILE COVERS 1907 - 22 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 21 Mar 2005 (20050321/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

9 L1
68456 DIMETHYLAMINO
1 DIMETHYLAMINOS
68457 DIMETHYLAMINO
(DIMETHYLAMINO OR DIMETHYLAMINOS)
84608 PROPYL
5 PROPYLS
84611 PROPYL
(PROPYL OR PROPYLS)
146526 PR
1802 PRS
147678 PR
(PR OR PRS)
217114 PROPYL
(PROPYL OR PR)
18811 TRIHYDROXY

568 CHOLAN
118292 AMIDE
74906 AMIDES
161409 AMIDE

(AMIDE OR AMIDES)

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L2 9 L1 OR DIMETHYLAMINO (L) PROPYL (L) TRIHYDROXY (L) CHOLAN (L) AMIDE OR
MCHAPSO

=> d 1-9 cbib abs hitstr

L2 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS ON STN
 2001:748108 Document No. 135:300482 Isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence assay for
 γ-secretase activity and inhibitors. Roberts, Susan B.; Hendrick,
 Joseph P.; Vinitsky, Alexander; Lewis, Martin; Smith, David W.; Pak,
 Roger
 (Bristol-Myers Squibb Company, USA). PCT Int. Appl. WO 2001075435 A2
 20011011, 127 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA,
 BB, BG, BR, BY, BE, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, ES, ES,
 FI, GB, GD, GE, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ,
 CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,
 ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2.
 APPLICATION: WO 2001-US10453 20010330. PRIORITY: US 2000-PV194495
 20000403.

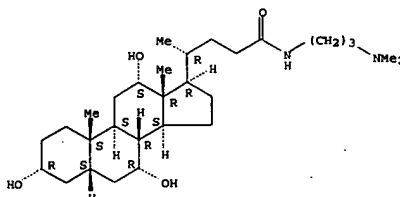
AB The present invention provides an isolated, functionally-active protein
 that catalyzes cleavage of a γ-secretase substrate. The functional
 activity of the isolated protein suggests that the isolated protein
 includes γ-secretase. In one embodiment, the isolated
 γ-secretase protein is associated with presenilin 1. The present
 invention also relates to homogeneous methods for monitoring cleavage of
 β-amyloid precursor protein (BAPP) by γ-secretase, wherein
 the steps of isolating and retrieving cleavage products have been
 eliminated. Cleavage can be detected by binding a pair of fluorescent
 adducts to the γ-cleaved BAPP fragment. Preferably, a first
 fluorescent adduct binds to the carboxy-terminal end of the
 γ-cleaved BAPP fragment, with substantially no cross-reactivity
 to uncleaved BAPP or to other types of γ-cleaved BAPP
 fragments, while a second fluorescent adduct binds to a portion within
 the amino-terminal region on the γ-cleaved BAPP fragment.
 Detection of binding to the γ-cleaved BAPP fragment is determined by
 monitoring the fluorescent energy transfer between the adducts.

IT 74555-98-1
 RL: NNU (Other use, unclassified); USES (Uses)
 (solubilizer; isolation of functionally active γ-secretase
 presenilin 1 complex and fluorescence assay for γ-secretase
 activity and inhibitors)

RN 74555-98-1 HCAPLUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
 (3a,5b,7a,12a)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L2 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)



L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS ON STN
 1997:21100 Document No. 126:75132 Design and Synthesis of Molecular
 Umbrellas. Janout, Vaclav; Lanier, Marion; Regen, Steven L. (Department
 of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA). Journal of
 the American Chemical Society, 119(4), 640-647 (English) 1997. CODEN:
 JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB The design and synthesis of a series of conjugates derived from cholic
 acid, spermidine, and 5-(dimethylamino)-1-naphthalenesulfonyl (dansyl),
 which effectively shield the dansyl moiety from water is described.
 Direct coupling of cholic acid to both terminal amino groups of
 spermidine, and attachment of the environmentally-sensitive dansyl moiety
 to the remaining secondary amine, yields a mol. umbrella (I) whose
 fluorescent properties (λ_{max} and emission intensity) reflect a
 nonpolar microenvironment in water and one that is relatively polar in
 intermediate dimethoxyethane/water mixts. Comparison of I with analogous
 single-walled and no-walled umbrellas further indicates that a min. of
 two walls is necessary in order to have umbrella-like properties.

Examination of the fluorescent properties of a related double-walled umbrella, bearing a
 flexible (2-hydroxyethyl)carbamate moiety at the C-3 position of the
 sterol, reveals that umbrella-like properties are present even when
 facial amphiphilicity is not rigorously maintained; however, the mol.'s ability
 to shield the fluorophore, as judged by its relative emission intensity,
 is diminished. Methyl-capping of the (2-hydroxyethyl)carbamate enhances
 the umbrella's ability to provide a hydrophobic shelter in water. A
 tetra-walled analog of I, bearing four cholic acid units, has been
 synthesized and its dansyl group has reduced exposure toward water. The
 potential utility of mol. umbrellas in the area of drug delivery is
 briefly discussed.

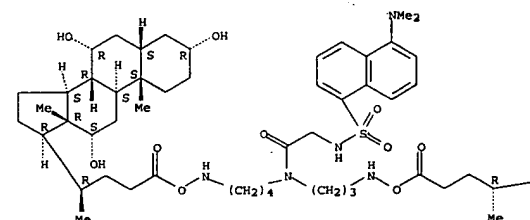
IT 185450-86-6P 185450-89-9P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (preparation of surfactant dansylaminoacetylbischoylspermidine
 deriva.)

RN 185450-86-6 HCAPLUS
 CN Acetamide, 2-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]-N-[4-
 {[[[3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-24-
 yl]oxy]amino]butyl]-N-[3-[[[3a,5b,7a,12a)-3,7,12-
 trihydroxy-24-oxocholan-24-yl]oxy]amino]propyl]- (9CI) (CA INDEX NAME)

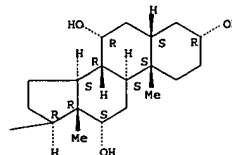
Absolute stereochemistry.

L2 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2005 ACS ON STN (Continued)

PAGE 1-A



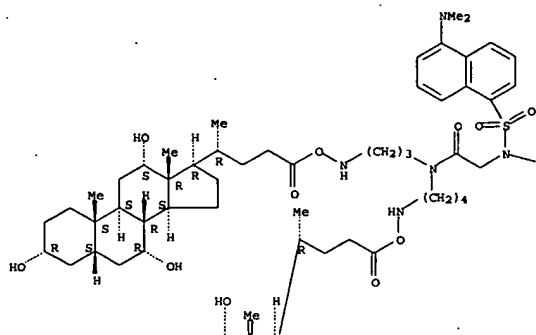
PAGE 1-B



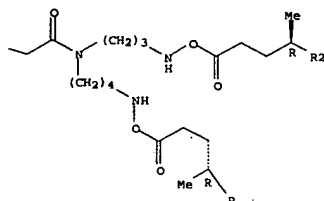
RN 185450-89-9 HCAPLUS
 CN Acetamide, 2-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]bis[N-
 {4-[[[3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-
 24-yl]oxy]amino]butyl]-N-[3-[[[3a,5b,7a,12a)-
 3,7,12-trihydroxy-24-oxocholan-24-yl]oxy]amino]propyl]- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L2 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
 1996:62571 Document No. 124:185506 Molecular umbrellas. Janout, Vaclav; Lanier, Marion; Regen, Steven L. (Department of Chemistry, Lehigh University, Bethlehem, PA, 18015, USA). Journal of the American Chemical Society, 118(6), 1573-4 (English) 1996. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

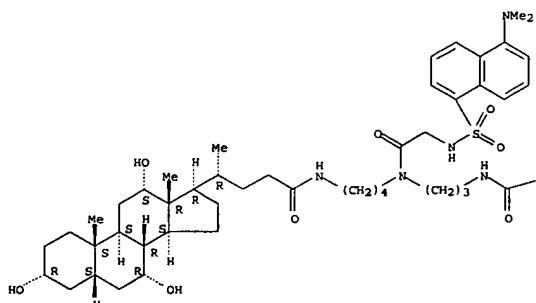
AB In this paper, a new concept in surfactant chemical is introduced that is based on mols. that mimic the structure and function of umbrellas; i.e., mols. that can cover an attached agent and shield it from an incompatible environment. A prototype "double-walled" umbrella has been synthesized using cholic acid as "wall material", spermidine as a scaffold, and an environmentally-sensitive, fluorescent probe, 5-dimethylamino-1-naphthalene sulfonyl (Dansyl) as the agent. Fluorescence measurements carried out in varying mixts. of dimethoxyethane/water reveal a "turning point"; i.e., a DMS/water ratio at which a min. fluorescence intensity is observed. In striking contrast, a single-walled analog and a control mol. do not exhibit a turning point; in these latter cases, the fluorescence continuously decreases as the water content increases. Potential applications of this new class of compds. in the areas of drug design and drug delivery are briefly discussed.

IT 174094-97-4P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (mol. umbrellas for drug delivery)

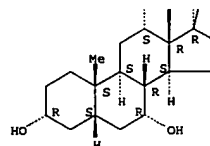
RN 174094-97-4 HCAPLUS
 CN Cholan-24-amide, N-[3-[[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]amino]acetyl]-4-[[[3a,5b,7a,12.alpha.-3,7,12-trihydroxy-, (3a,5b,7a,12a)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

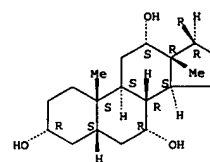
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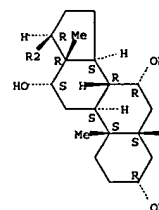
PAGE 2-A



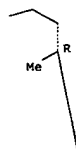
PAGE 3-A



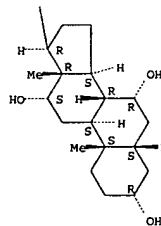
PAGE 4-A



PAGE 1-B

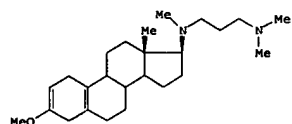


PAGE 2-B



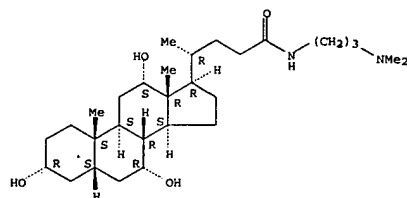
L2 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
 1988:75714 Document No. 108:75714 Steroids and their cyclic hydrocarbon
 analogs with amino-containing sidechains, useful as antidiabetic agents
 and inhibitors of phospholipase A2. Johnson, Roy A.; Bundy, Gordon L.;
 Youngdale, Gilbert A.; Morton, Douglas R. (Upjohn Co., USA). PCT Int.
 Appl. WO 8702367 A2 19870423, 177 pp. DESIGNATED STATES: W: JP, US, US;
 RW: AT, BS, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXX02.
 APPLICATION: WO 1986-US2116 19861007. PRIORITY: US 1985-788995 19851018;
 US 1986-843120 19860324.

GI

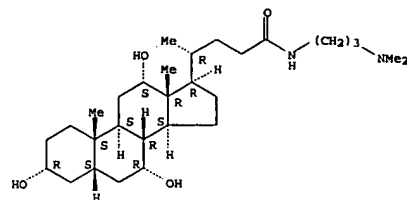


AB A wide variety of steroids and nonsteroidal analogs bearing
 amino-containing
 sidechains were prepared for use as antidiabetic agents and in the
 treatment
 or prevention of phospholipase A2-mediated conditions. Reductive
 amination of estrone Me ether with Me₂N(CH₂)₃NH₂ and HCO₂H at
 160-170° gave N-[3-(dimethylamino)propyl]-N-formyl-3-methoxyestra-
 1,3,5(10)-trien-17β-amine, which was reduced by LiAlH₄ in dioxane to
 the N-Me derivative. This underwent Birch reduction, followed by 3
 recrystns. in
 Et₂O-MeCN, to give estradienamine derivative I. In the perfused guinea
 pig
 lung, I completely inhibited phospholipase A2 at 4 × 10⁻⁷ M.
 IT 76555-98-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reaction of, in synthesis of phospholipase
 A2-inhibiting
 amino steroids and analogs)
 RN 76555-98-1 HCAPLUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
 (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.

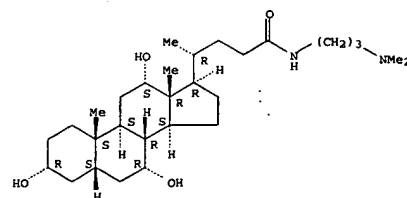
L2 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
 1986:187118 Document No. 104:187118 Fixed steroids. Itagaki, Koji; Ito,
 Takeshi; Ando, Kyoto (Mitsubishi Chemical Industries Co., Ltd., Japan).
 Jpn. Kokai Tokkyo Koho JP 60133005 A2 19850716 Showa, 6 pp. (Japanese).
 CODEN: JYXXAP. APPLICATION: JP 1983-241342 19831221.
 AB Products useful as carriers in affinity chromatog. are prepared by
 amidation
 of carboxylated steroids with polyalkylenepolyamines and reaction of the
 amides with insol. matrix polymers having amine-reactive groups. Thus,
 heating 20 g Et cholate with 100 g Me₂N(CH₂)₃NH₂ 16 h at 140° gave
 21.1 g amide. Heating 19.4 g amide and 5 g chloromethylated
 styrene-divinylbenzene polymer in 1:1 dioxane-MeOH for 16 h at 70°
 gave 10.3 g fixed steroid (ion exchange volume 1.08 mequiv/g dry resin).
 IT 76555-98-1D, reaction products with chloromethylated styrene
 copolymers
 RL: USES (Uses)
 (carriers in affinity chromatog.)
 RN 76555-98-1 HCAPLUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
 (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.



L2 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L2 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2005 ACS on STN
 1983:402687 Document No. 99:2687 Sulfobetaine derivatives of bile acids:
 nondenaturing surfactants for membrane biochemistry. Hjelmeland, Leonard
 M.; Hebert, Daniel W.; Osborne, James C., Jr. (Dev. Pharmacol. Branch,
 Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA).
 Analytical
 Biochemistry, 130(1), 72-82 (English) 1983. CODEN: ANBCA2. ISSN:
 0003-2697.
 AB The syntheses of 4 new sulfobetaine derivs. of bile salts are presented,
 along with a general set of criteria for useful detergents in membrane
 biochem. Phys. properties including the critical micelle concentration,
 aggregation
 number, partial sp. volume, critical micellar temperature, UV-visible
 spectrum, and CD
 spectrum were examined for the new compds. To examine the interaction of
 this class of compds. with macromols., CHAPS was further studied. CD
 spectra of apolipoprotein C-II12 were measured in the presence of varying
 concns. of CHAPS to determine the effect of this compound on secondary
 structure.
 Gel-exclusion chromatog. and sedimentation equilibrium studies of
 cytochrome P
 450 in the presence of CHAPS was also performed to establish the ability
 of this detergent to disaggregate cytochrome P 450 to a monomeric/dimeric
 state.
 IT 76555-98-1P
 RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and alkylation of)
 RN 76555-98-1 HCAPLUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
 (3α,5β,7α,12α)- (9CI) (CA INDEX NAME)
 Absolute stereochemistry.



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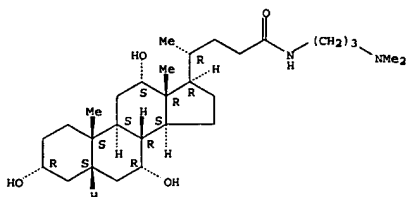
L2 ANSWER 7 OF 9 HCAPIUS COPYRIGHT 2005 ACS on STN
 1982:452173 Document No. 97:52173 Nondenaturing zwitterionic detergents for membrane biochemistry. Hjelmeland, Leonard (United States Dept. of Health and Human Services, USA). U. S. Pat. Appl. US 294203 A0 19820409, 47 pp. Avail. NTIS Order No. PAT-APPL-6-294 203 (English). CODEN: XAXXAV. APPLICATION: US 1981-294203 19810826.

AB Preparation of 2 nondenaturing zwitterionic detergents, 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS) and 3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate (CHAPSO), is described for solubilization of membrane proteins. CHAPSO was 2-fold more effective in solubilizing active opiate receptors than CHAPS.

IT 76555-98-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reactions of, with propanesultone or sodium chlorohydroxypropanesulfonate)

RN 76555-98-1 HCAPIUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



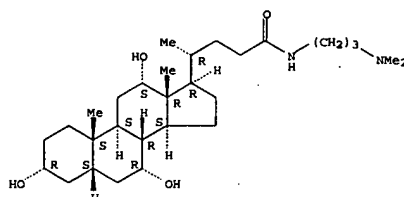
L2 ANSWER 8 OF 9 HCAPIUS COPYRIGHT 2005 ACS on STN
 1981:438693 Document No. 95:38693 Nondenaturing zwitterionic detergents for membrane biochemistry. Hjelmeland, Leonard M. (United States Dept. of Health, Education, and Welfare, USA). U. S. Pat. Appl. US 181465 19810327, 22 pp. Avail. NTIS Order No. PAT-APPL-181 465. (English). CODEN: XAXXAV. APPLICATION: US 1980-181465 19800826.

AB Preparation of zwitterionic detergents, which are a combination of a bile salt hydrophobic group and a sulfobetaine-type polar group, is described for solubilizing membrane proteins in a nondenatured state. 3-[(3-Cholamidopropyl)dimethylammonio]-1-propanesulfonate (I) preparation is described. The Et3NH+ salt of cholic acid was formed in THF, then ethylchloroformate was added to precipitate Et3NHCl, which was removed from the mixed anhydride by filtration. The mixed anhydride reacted with 3-dimethylaminopropylamine to form N-(3-dimethylaminopropyl)cholamide (II), EtOH, and CO2. In the final step, the tertiary amine group of II reacted with propane sultone to give the sulfobetaine, I. The yield was 75-80% theor., and the purity of I was >95% as judged by TLC.

IT 76555-98-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction of, with propanesultone)

RN 76555-98-1 HCAPIUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

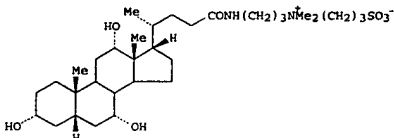
Absolute stereochemistry.



*

L2 ANSWER 9 OF 9 HCAPIUS COPYRIGHT 2005 ACS on STN
 1981:79812 Document No. 94:79812 A nondenaturing zwitterionic detergent for membrane biochemistry: Design and synthesis. Hjelmeland, Leonard M. (Dev. Pharmacol. Branch, Natl. Inst. Child Health Hum. Dev., Bethesda, MD, 20205, USA). Proceedings of the National Academy of Sciences of the United States of America, 77(11), 6368-70 (English) 1980. CODEN: PHASAA. ISSN: 0027-8424.

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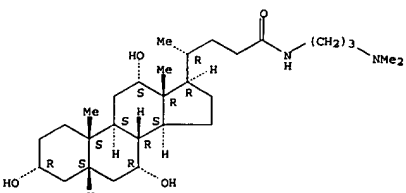


AB The synthesis and evaluation of a new detergent that is a zwitterionic derivative (I) of cholic acid is presented. This detergent combines the useful properties of both the sulfobetaine-type detergents and the bile salt anions. The new detergent proved to be effective at solubilizing membrane proteins in a nondenatured state.

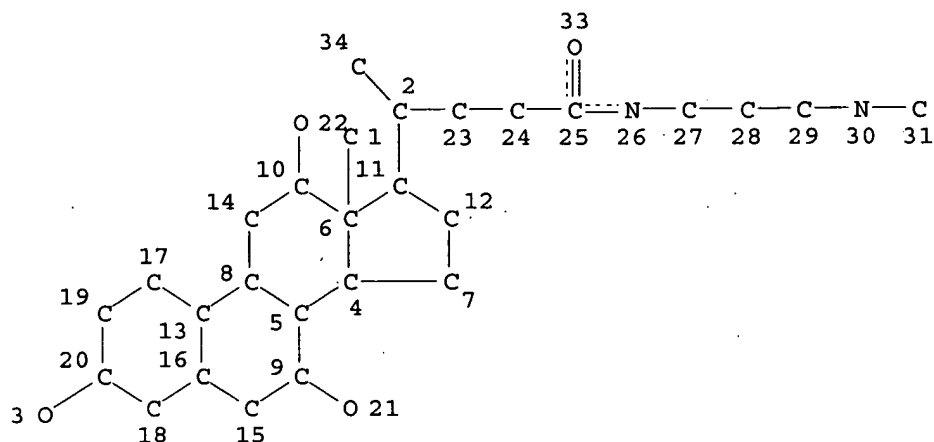
IT 76555-98-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reaction with propanesultone)

RN 76555-98-1 HCAPIUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-, (3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L5 STR.



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 375 ITERATIONS
SEARCH TIME: 00.00.01

98 ANSWERS

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	ENTRY	SESSION
FULL ESTIMATED COST	165.32	250.83
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-6.57

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FILE COVERS 1907 - 22 Mar 2005 VOL 142 ISS 13
FILE LAST UPDATED: 21 Mar 2005 (20050321/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L8 1067 L7

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pal r?/au

L9 1979 ROBERTS S?/AU

L10 205 HENDRICK J?/AU

L11 20 VINITSKY A?/AU

L12 2390 LEWIS M?/AU

L13 14724 SMITH D?/AU

L14 561 PAL R?/AU

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L14 249 PAK R?/AU

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L15 3 L8 AND (L9 OR L10 OR L11 OR L12 OR L13 OR L14)

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D15 ANSR 1 OF 3 RECAPS: CUMIRIGHT: BUS: 20000728
2002: 107078 DocId:313615600 Novel methods and compositions to
upregulate, redirect or limit immune responses to peptides, proteins and
other bioactive components and vectors expressing the same. Bot, Adrian;
Dellamary, Luis; Smith, Dan J.; Woods, Catherine M. (Alliance
Pharmaceutical Corp., USA). PCT Int. Appl. WO 2002009674 A2 20020207, 80
pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG,
BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DK, DK, DM, DE, EC,
EE, ES, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, LC, LC, LR, LS, LT, LU, LV, MA, MG, MK, MN, MM, MX,
MZ, NO, NR, NZ, PT, RO, RU, SD, SE, SI, SK, SK, SL, TJ, TM, TR,
TZ, UA, UG, UZ, VE, VN, YU, ZA, ZM, ZW. PCT No. P02/009674.
Int. Cl. B6: BF, BF, CF, CC, CH, CI, CN, CY, DE, DE, FR, FR, GB, GR,
IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English).
CODEN: P1XXD2. APPLICATION: WO 2001:US246038 20010730. PRIORITY: US
2000-PV221544 20000728.

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AB Novel compounds are disclosed which can induce or enhance an immune response against foreign or self antigens (microbial or parasitic) or modulate (suppress) the activity of pathogenic cells in inflammatory or autoimmune diseases. Compounds and methods are taught in how to limit the generation of an immune response against formulated peptides and proteins with application to cancer or hormonal therapy. The use of the therapy of suppressing autoimmunity are also disclosed which use ligands for cellular receptors expressed on cells of the innate immune system and

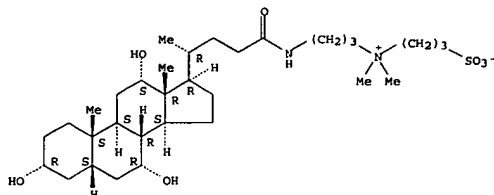
more specifically for down-regulation of autoimmune processes by either deletion or induction of energy at the level of autoreactive T cells or triggering active-suppressor T cells that down-regulate the activity of pathogenic cells.

IT 75621-03-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(novel methods and compounds, to modulate and control immune responses

and immune disorders)

RN 75621-03-3 HCAPLUS
 CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-
 -[(3 α ,5 β ,7 α ,12 α)-3,7,12-trihydroxy-24-oxocholan-24-
 -yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN

2001:748108 Document No. 135:300482 Isolation of functionally active
 γ-secretase presenilin 1 complex and fluorescence assay for
 γ-secretase activity and inhibitors. Roberts, Susan B.;
 Hendrick, Joseph P.; Vinitzky, Alexander; Lewis, Martin;
 Smith, David W.; Pak, Roger
 (Bristol-Myers Squibb Company, USA) PCT Int. Appl. WO 2001/075345 A2
 20011217:127-131. PCT Int. Cl. 6: A61M 35/00, A61K 47/32, A61K 48/00,
 BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES,
 FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
 LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NZ, PL,
 PT, RU, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, MG, MN, MW, RU, TJ, TM; RW: AT, BE, BF, BJ,
 CF, CG, CH, CI, CM, CY, DE, DK, EE, FI, FR, GA, GB, GR, IE, IT, LJ, MK,
 NL, NR, NI, NG, NL, PT, SE, SN, SD, TG, TR, (English) PCT FILING DATE
 APPLICATION: WO 2001-051045 20010330. PRIORITY: US 2000-PV194495
 A9900403.

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ -secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ -secretase. In one embodiment, the isolated γ -secretase protein is associated with presenilin 1. The present invention also relates to a homogeneous or heterogeneous monitoring cleavage of β -amyloid precursor protein (BAPP) by γ -secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ -cleaved BAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ -cleaved BAPP fragment, with substantially no reactivity to uncleaved BAPP or to other types of γ -cleaved BAPP fragments, while a second fluorescent adduct binds to a portion within

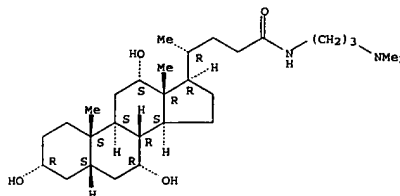
Detection of binding to the γ -cleaved β APP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT 76555-98-1
RL: NUU (Other use, unclassified); USES (Uses)
(solubilizer; isolation of functionally active γ -secretase
presenilin 1 complex and fluorescence assay for γ -secretase
activity and inhibitors)

RN 76555-98-1 HCAPLUS
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L15 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN (Continued)



L15 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
 1996:367800 Document No. 125:31908 Buffer system for increasing
 seroconversion efficiency. Smith, Daniel S.; Walker, John C.
 (Curators of the University of Missouri, USA). PCT Int. Appl. WO 9607318
 A1 19960314, 72 pp. DESIGNATED STATES: M; AU, CA, JP; RM: AT, BE, CH,
 DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN:
 PIXXD2. APPLICATION: WO 1995-US11462 19950907. PRIORITY: US 1994-303156
 19940908.

AB A method of increasing efficiency of deantigenation of blood group
 epitopes on erythrocytes (seroconversion) by exoglycosidases utilizing a
 step of performing the deantigenation in a zwitterionic buffer. The
 method provides a buffer system and exoglycosidase that utilized a twenty
 to one hundred fold lower total enzyme mass than the prior art methods.
 Zwitterions are selected from glycine, alanine, CHAPS, etc., and
 exoglycosidases are selected from Glycine max α -D-galactosidase,
 Gallus domesticus α -N-acetylgalactosaminidase, Phaseolus vulgaris
 α -N-acetyl-galactosidase and other multimeric eucaryotic
 exoglycosidases.

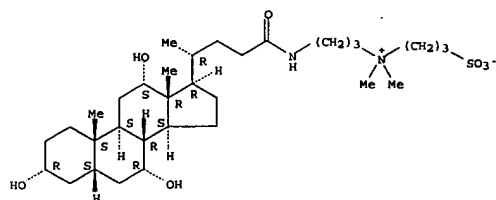
IT 75621-03-3, CHAPS

RL: MQA (Modifier or additive use); USES (Uses)
 (zwitterion buffer and exoglycosidases for increasing efficiency of
 deantigenation of blood group epitopes on erythrocytes or
 seroconversion)

RN 75621-03-3 HCAPLUS

CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-
 [[[(3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-24-
 yl]aminol-], inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L16 1 L9 AND L10 AND L11 AND L12 AND L13 AND L14

```

=> s l16 not l15
L17      0 L16 NOT L15

=> s l8 and ((g or gamma) (w)secret? or protein cocplex)
      2738524 G
      772898 GAMMA
      4935 GAMMAS
      773055 GAMMA
            (GAMMA OR GAMMAS)
      320371 SECRET?
      2896 (G OR GAMMA) (W) SECRET?
      1724457 PROTEIN
      1196534 PROTEINS
      2002147 PROTEIN
            (PROTEIN OR PROTEINS)
      7 COCMPLX
      4 COCMPLXES
      11 COCMPLX
            (COCMPLX OR COCMPLXES)
      0 PROTEIN COCMPLX
            (PROTEIN (W) COCMPLX)
L18      6 L8 AND ((G OR GAMMA) (W) SECRET? OR PROTEIN COCMPLX)

=> s l18 not (l15 or l16)
L19      5 L18 NOT (L15 OR L16)

=> d 1-5 cbib abs hitstr

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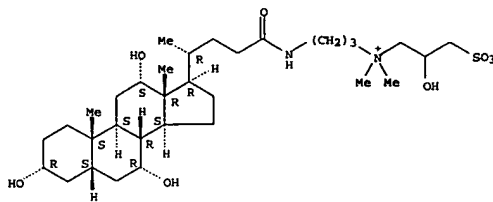
the Human γ -Secretase Complex. Fraering, Patrick C.; Ye, Wenjuan; Strub, Jean-Marc; Dolios, Georgia; LaVoie, Matthew J.; Oatassewski, Beth L.; van Dorsselaer, Alain; Wang, Rong; Selkoe, Dennis J.; Wolfe, Michael S. (Center for Neurologic Diseases, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 02115, USA). Biochemistry, 43(30), 9774-9789 (English) 2004. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB γ -Secretase is a member of an unusual class of proteases with intramembrane catalytic sites. This enzyme cleaves many type I membrane proteins, including the amyloid β -protein (A β) precursor (APP) and the Notch receptor. Biochem. and genetic studies have identified four membrane proteins as components of γ -secretase: heterodimeric presenilin (PS) composed of its N- and C-terminal fragments (PS-NTF/CTF), a mature glycosylated form of nicastrin (NCT), Aph-1, and Pen-2. Recent data from studies in *Drosophila*, mammalian, and yeast cells suggest that PS, NCT, Aph-1, and Pen-2 are necessary and sufficient to reconstitute γ -secretase activity. However, many unresolved issues, in particular the possibility of other structural or regulatory components, would be resolved by actually purifying the enzyme. Here, we report a detailed, multistep purification procedure for active γ -secretase and an initial characterization of the purified protease. Extensive mass spectrometry of the purified proteins strongly suggests that PS-NTF/CTF, mNCT, Aph-1, and Pen-2 are the components of active γ -secretase. Using the purified γ -secretase, we describe factors that modulate the production of specific A β species: (1) phosphatidylcholine and sphingomyelin dramatically improve activity without changing cleavage specificity within an APP substrate; (2) increasing CHAPS concns. from 0.1 to 0.25% yields a ~100% increase in A β 42 production; (3) exposure of an APP-based recombinant substrate to 0.5M SDS modulates cleavage specificity from a disease-mimicking pattern (high A β 42/43) to a physiolo. pattern (high A β 40); and (4) sulindac sulfide directly and preferentially decreases A β 42 cleavage within the purified complex. Taken together, our results define a procedure for purifying active γ -secretase and suggest that the lipid-mediated conformation of both enzyme and substrate regulate the production of the potentially neurotoxic A β 42 and A β 43 peptides.

IT 82473-24-3, CHAPSO
RL: BSU (Biological study, unclassified); BIOL (Biological study) (CHAPSO and sodium dodecyl sulfate promotes amyloid β -protein precursor cleavage)

RN 82473-24-3 HCAPIUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[[3,5,8,7a,12a]-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



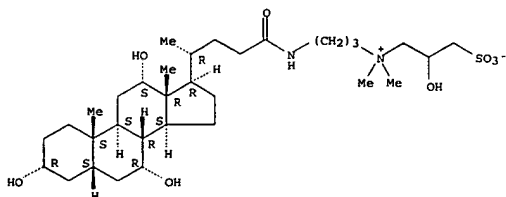
L19 ANSWER 2 OF 5 HCAPIUS COPYRIGHT 2005 ACS on STN
2004:504793 Document No. 141:50129 Assay for γ -secretase modulators. Behr, Dirk (Merck Sharp & Dohme Limited, UK). Brit. UK Pat. Appl. GB 2396415 A1 20040623, 30 pp. (English). CODEN: BAKXDU. APPLICATION: GB 2003-28875 20031212. PRIORITY: GB 2002-29582 20021219.

AB An assay for identifying compds. that interact with the γ -secretase complex comprising preparing and solubilizing a source of the complex, incubating a test compound together with an affinity probe and the source, capturing the resulting bound complex, and analyzing the components of the complex to determine whether the test compound has interacted with the complex by determining the amount of PS1-NTF, PS1-CTF or mature nicastrin present in the complex. The assay may be used in the identification of components of the γ -secretase complex.

IT 82473-24-3, CHAPSO
RL: ARU (Analytical role, unclassified); ANST (Analytical study) (assay for γ -secretase modulators)

RN 82473-24-3 HCAPIUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[[3,5,8,7a,12a]-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



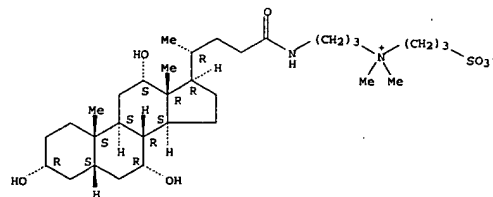
L19 ANSWER 3 OF 5 HCAPIUS COPYRIGHT 2005 ACS on STN
2003:173459 Document No. 138:217451 Preparation, substrate specificity, and therapeutic uses of human γ 3 protease involved in processing of amyloid precursor protein. Crouthamel, Ming-Chih; Gardell, Stephen J.; Huang, Qian; Lai, Ming-Tain; Li, Yueying (Merck & Co., Inc., USA). PCT Int. Appl. WO 2003018050 A1 20030306, 48 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US26969 20020808. PRIORITY: US 2001-PV311410 20010810.

AB The invention provides γ 3 protease, a novel aspartyl class protease that is capable of taking part in the processing of amyloid precursor protein (APP) to A β peptide. The γ 3 protease may be involved in the development and/or progression of Alzheimer's disease. It has a Mr of 60-120 kDa on gel filtration, and its activity is inhibited by pepstatin A but not by L685,458 (a known γ -secretase inhibitor) with a pH optimum of 6.0. γ 3 Protease cleaves amyloid precursor protein, as well as artificial substrates incorporating portions of APP695, at the same or similar sites as γ -secretase, but can be distinguished from the known γ -secretase activity involving presenilin-1 and presenilin-2. Methods of assaying γ 3 protease and identifying potential inhibitors, useful in the prevention or treatment of Alzheimer's disease, are disclosed.

IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
RL: NUU (Other use, unclassified); USRS (Uses) (preparation of γ 3 protease from biol. membranes in presence of; preparation, substrate specificity, and therapeutic uses of human γ 3 protease involved in processing of amyloid precursor protein)

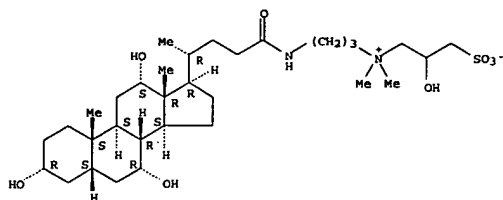
RN 75621-03-3 HCAPIUS
CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfopropyl)-3-[[[3,5,8,7a,12a]-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82473-24-3 HCAPIUS
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[[[3,5,8,7a,12a]-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



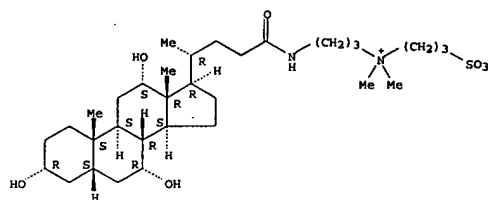
L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
 2001:816967 Document No. 135:354692 γ -Secretase substrates and in vitro assays. Li, Yue-Ming; Xu, Min; Huang, Qian; Gardell, Stephen (Merck & Co., Inc., USA). PCT Int. Appl. WO 2001083811 A1 20011108, 36 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LJ, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US13332 20010425. PRIORITY: US 2000-PV201053 20000501.

AB The present invention features γ -secretase substrates and in vitro assays for measuring γ -secretase activity employing such substrates. The γ -secretase substrates described herein contain a hydrophilic polypeptide moiety (Asp-Tyr-Lys-Asp-Asp-Asp-Lys) covalently joined to the C-terminus of a β -CTF domain. A " β -CTF domain" is a polypeptide that can be cleaved by γ -secretase and which approximates the C-terminal fragment (amino acids 596-695) of human amyloid precursor protein (APP) produced after cleavage of APP by a β -secretase, or is a functional derivative thereof. The hydrophilic polypeptide is chosen to increase the solubility of the γ -secretase substrate in a zwitterionic detergent. Thus, a fusion protein consisting sequentially of an N-terminal Met, human APP(597-695), and the Flag tag sequence is processed by γ -secretase. The A β 40 and A β 42-related products are detected by electrochemiluminescence using biotinylated 4G8 antibody and ruthenylated G2-10 or FCA3542, resp.

IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
 RL: ARU (Analytical role, unclassified); ANST (Analytical study) (zwitterionic detergent; γ -secretase substrates and in vitro assays)

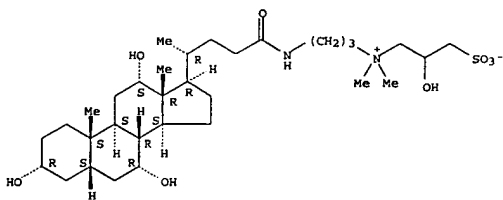
RN 75621-03-3 HCAPLUS
 CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfo-3-[[[(3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82473-24-3 HCAPLUS
 CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[[[(3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
 2000:392881 Document No. 133:146729 Presenilin 1 is linked with γ -secretase activity in the detergent solubilized state. Li, Yue-Ming; Lai, Ming-Tain; Xu, Min; Huang, Qian; DiMuzio-Mower, Jillian; Gardana, Mohinder K.; Shi, Xiao-Ping; Yin, Kuo-Chang; Shafer, Jules A.; Gardell, Stephen J. (Department of Biological Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA). Proceedings of the National Academy of Sciences of the United States of America, 97(11), 6138-6143 (English) 2000. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

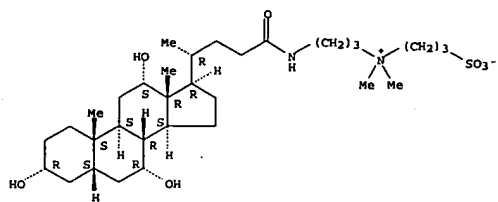
AB γ -Secretase is a membrane-associated protease that cleaves within the transmembrane region of amyloid precursor protein to generate the C termini of the two A β peptide isoforms, A β 40 and A β 42. Here we report the detergent solubilization and partial characterization of γ -secretase. The activity of solubilized γ -secretase was measured with a recombinant substrate, C100Flag, consisting largely of the C-terminal fragment of amyloid precursor protein downstream of the β -secretase cleavage site. Cleavage of C100Flag by γ -secretase was detected by electrochemiluminescence using antibodies that specifically recognize the A β 40 or A β 42 termini. Incubation of C100Flag with HeLa cell membranes or detergent-solubilized HeLa cell membranes generates both the A β 40 and A β 42 termini. Recovery of catalytically competent, soluble γ -secretase critically depends on the choice of detergent: CHAPSO (3-[(3-cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate) but not Triton X-100 is suitable. Solubilized γ -secretase activity is inhibited by pepstatin and more potently by a novel aspartyl protease transition-state analog inhibitor that blocks formation of A β 40 and A β 42 in mammalian cells. Upon gel exclusion chromatog., solubilized γ -secretase activity coelutes with presenilin 1 (PS1) at an apparent relative mol. weight

of approx. 2.0×10^6 . Anti-PS1 antibody immunoprecipitates γ -secretase activity from the solubilized γ -secretase preparation. These data suggest that γ -secretase activity is catalyzed by a PS1-containing macromol. complex.

IT 75621-03-3, CHAPS 82473-24-3, CHAPSO
 RL: NUU (Other use, unclassified); USES (Uses) (presenilin 1 is linked with γ -secretase activity in the detergent-solubilized state)

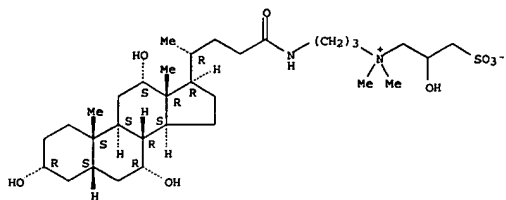
RN 75621-03-3 HCAPLUS
 CN 1-Propanaminium, N,N-dimethyl-N-(3-sulfo-3-[[[(3a,5b,7a,12a)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 82473-24-3 HCAPLUS
 CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[(3 α ,5 β ,7 α ,12 α)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> s l8 and secretase
1795 SECRETASE
288 SECRETASES
1852 SECRETASE
(SECRETASE OR SECRETASES)
L20 6 L8 AND SECRETASE

=> s l20 not (l19 or l15 or l16)
L21 0 L20 NOT (L19 OR L15 OR L16)

=> del his y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	54.22	305.05
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.84	-12.41

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STRUCTURE FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1
DICTIONARY FILE UPDATES: 20 MAR 2005 HIGHEST RN 845957-95-1

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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FILE 'HCAPLUS' ENTERED AT 16:53:03 ON 18 MAR 2005

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E HENDRICK JOSEPH P/AU
L59 23 SEA ABB=ON ("HENDRICK JOSEPH"/AU OR "HENDRICK JOSEPH P"/AU OR
"HENDRICK JOSEPH P JR"/AU OR "HENDRICK JOSEPH PATRICK"/AU)
E VINITSKY ALEXANDER/AU
L60 20 SEA ABB=ON ("VINITSKY A"/AU OR "VINITSKY A H"/AU OR "VINITSKY
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L61 6 SEA ABB=ON "LEWIS MARTIN A"/AU
E SMITH DAVID W/AU
L62 179 SEA ABB=ON ("SMITH DAVID W"/AU OR "SMITH DAVID W E"/AU OR
"SMITH DAVID WALLACE"/AU OR "SMITH DAVID WALTER"/AU OR "SMITH
DAVID WARREN"/AU OR "SMITH DAVID WAYNE"/AU)
E PAK ROGER HOCHOON/AU
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L66 7 SEA ABB=ON L64 AND ?GAMMA?(W)?SECRETASE?
L67 1 SEA ABB=ON L66 AND ?ISOLATION?
SELECT RN L67 1-1

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search*

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OR 199164-91-5/BI OR 2321-07-5/BI OR 247144-99-6/BI OR
262412-30-6/BI OR 264902-77-4/BI OR 304014-12-8/BI OR 366488-00
-8/BI OR 366488-01-9/BI OR 366520-85-6/BI OR 366520-86-7/BI OR
366522-28-3/BI OR 366522-29-4/BI OR 366801-12-9/BI OR 366801-14
-1/BI OR 50402-56-7/BI OR 6268-49-1/BI OR 70281-37-7/BI OR
7440-33-7/BI OR 7440-53-1/BI OR 7440-63-3/BI OR 76555-98-1/BI
OR 7782-39-0/BI OR 81-88-9/BI OR 91-64-5/BI)

FILE 'HCAPLUS' ENTERED AT 16:55:52 ON 18 MAR 2005

L69 1 SEA ABB=ON L67 AND L68

FILE 'REGISTRY' ENTERED AT 17:00:18 ON 18 MAR 2005

E CHAPSO/CN
E MCHAPSO/CN
L70 1 SEA ABB=ON CHAPSO/CN

FILE 'HCAPLUS' ENTERED AT 17:02:24 ON 18 MAR 2005

L71 0 SEA ABB=ON MCHAPSO
L72 0 SEA ABB=ON ?MCHAPSO?

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E N-3-DIMETHYLAMINOPROPYL/CN
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E CHOLANE/CN
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E CHOLAN-2-AMIDE/CN
E CHOLANAMIDE/CN
L74 1 SEA ABB=ON CHOLANAMIDE/CN
L75 STRUCTURE 26665-96-3
L76 0 SEA SSS SAM L75

L77
L78

12 SEA SSS FUL L75
1 SEA ABB=ON 76555-98-1/RN

See attachment (B)

FILE 'HCAPLUS' ENTERED AT 17:27:09 ON 18 MAR 2005

L79

7 SEA ABB=ON L78

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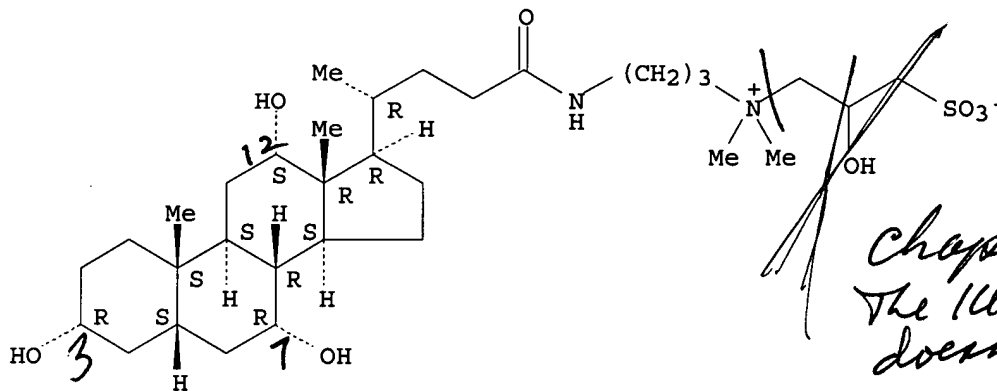
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Nichols 10/713,981

18/03/2005

L70 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 82473-24-3 REGISTRY
CN 1-Propanaminium, 2-hydroxy-N,N-dimethyl-3-sulfo-N-[3-
[[[(3 α ,5 β ,7 α ,12 α)-3,7,12-trihydroxy-24-oxocholan-24-
yl]amino]propyl]-, inner salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cholane, 1-propanaminium deriv.
OTHER NAMES:
CN 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate
CN **CHAPSO**
FS STEREOSEARCH
DR 120893-60-9
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CAPLUS, CHEMCATS, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MRCK*, MSDS-OHS,
PIRA, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA Caplus document type: Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC
(Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



185 REFERENCES IN FILE CA (1907 TO DATE)

185 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

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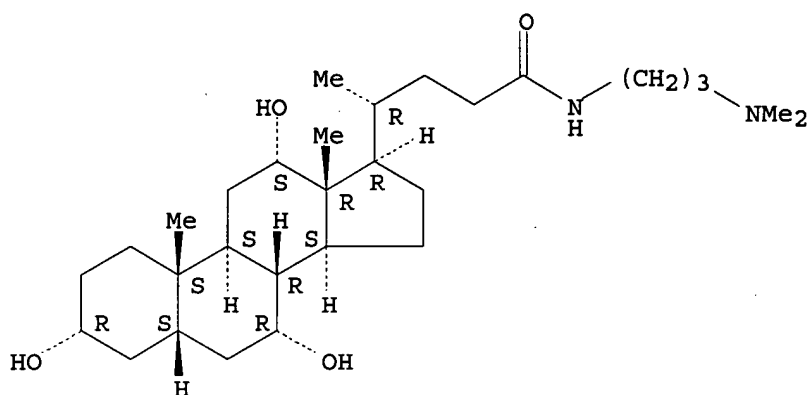
Nichols 10/713,981

18/03/2005

=> d

L78 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 76555-98-1 REGISTRY
CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
(3 α ,5 β ,7 α ,12 α)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H52 N2 O4
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAPLUS document type: Journal; Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent);
USES (Uses)
RLD.P Roles for non-specific derivatives from patents: USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ED Entered STN: 16 Nov 1984

This structure matches The IUPAC name given.

=> d ibib abs hitstr l69 1-1

L69 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2001:748108 HCAPLUS
 DOCUMENT NUMBER: 135:300482
 TITLE: Isolation of functionally active .
 gamma.-secretase presenilin 1
 complex and fluorescence assay for γ -
 secretase activity and inhibitors
 INVENTOR(S): Roberts, Susan B.; Hendrick, Joseph
 P.; Vinitzky, Alexander; Lewis, Martin;
 Smith, David W.; Pak, Roger
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001075435	A2	20011011	WO 2001-US10453	20010330
WO 2001075435	A3	20020808		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2405332	AA	20011011	CA 2001-2405332	20010330
US 2002025540	A1	20020228	US 2001-823153	20010330
US 6713248	B2	20040330		
EP 1305634	A2	20030502	EP 2001-922976	20010330
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004505608	T2	20040226	JP 2001-572863	20010330
US 2004121411	A1	20040624	US 2003-713981	20031114
PRIORITY APPLN. INFO.:			US 2000-194495P	P 20000403
			US 2001-823153	A3 20010330
			WO 2001-US10453	W 20010330

AB The present invention provides an isolated, functionally-active protein that catalyzes cleavage of a γ -secretase substrate. The functional activity of the isolated protein suggests that the isolated protein includes γ -secretase. In one embodiment, the isolated γ -secretase protein is associated with presenilin 1. The present invention also relates to homogeneous methods for monitoring cleavage of β -amyloid precursor protein (BAPP) by γ -secretase, wherein the steps of isolating and retrieving cleavage products have been eliminated. Cleavage can be detected by binding a pair of fluorescent adducts to the γ -cleaved BAPP fragment. Preferably, a first fluorescent adduct binds to the carboxy-terminal end of the γ -cleaved BAPP fragment, with substantially no cross-reactivity to uncleaved BAPP or to other types of γ -cleaved BAPP fragments, while a second fluorescent adduct binds to a portion within the amino-terminal region on the γ -cleaved BAPP fragment. Detection of binding to the

γ -cleaved BAPP fragment is determined by monitoring the fluorescent energy transfer between the adducts.

IT 366522-28-3

RL: PRP (Properties)

(Unclaimed; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)

RN 366522-28-3 HCAPLUS

CN 24: PN: WO0175435 SEQID: 7 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 262412-30-6P 366520-86-7P

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)

RN 262412-30-6 HCAPLUS

CN Amyloid precursor protein (synthetic human C-terminal fragment 100-amino acid precursor) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 366520-86-7 HCAPLUS

CN Amyloid precursor protein (synthetic human isoform C-83) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 7440-33-7, Tungsten, analysis 7782-39-0, Deuterium, analysis

RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(deuterium-tungsten lamp; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)

RN 7440-33-7 HCAPLUS

CN Tungsten (8CI, 9CI) (CA INDEX NAME)

W

RN 7782-39-0 HCAPLUS

CN Deuterium (7CI, 8CI, 9CI) (CA INDEX NAME)

D-D

IT 7440-63-3, Xenon, analysis

RL: ARU (Analytical role, unclassified); DEV (Device component use); ANST (Analytical study); USES (Uses)
(flash lamp; **isolation** of functionally active γ -**secretase** presenilin 1 complex and fluorescence assay for γ -**secretase** activity and inhibitors)

RN 7440-63-3 HCAPLUS

CN Xenon (8CI, 9CI) (CA INDEX NAME)

Xe

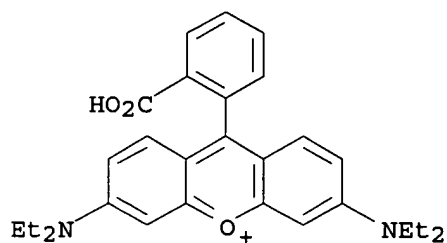
IT 338454-52-7DP, γ -Secretase, complexes
with presenilin 1
RL: ANT (Analyte); PRP (Properties); PUR (Purification or recovery); THU
(Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(isolation of functionally active γ -
secretase presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)
RN 338454-52-7 HCAPLUS
CN γ -Secretase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

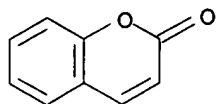
IT 338454-52-7, γ -Secretase
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(isolation of functionally active γ -
secretase presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)
RN 338454-52-7 HCAPLUS
CN γ -Secretase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 81-88-9 91-64-5, Coumarin 2321-07-5,
Fluorescein 6268-49-1 7440-53-1D, Europium, cryptates,
biological studies 50402-56-7, EDANS 70281-37-7,
Tetramethylrhodamine 146368-14-1 146368-16-3
247144-99-6 304014-12-8D, salts
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(isolation of functionally active γ -
secretase presenilin 1 complex and fluorescence assay for
 γ -secretase activity and inhibitors)
RN 81-88-9 HCAPLUS
CN Xanthylum, 9-(2-carboxyphenyl)-3,6-bis(diethylamino)-, chloride (9CI)
(CA INDEX NAME)

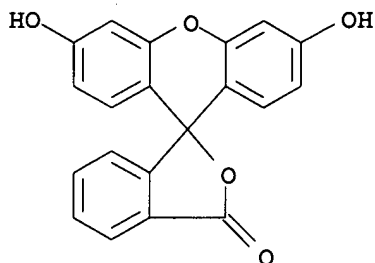
● Cl⁻

RN 91-64-5 HCAPLUS
CN 2H-1-Benzopyran-2-one (9CI) (CA INDEX NAME)



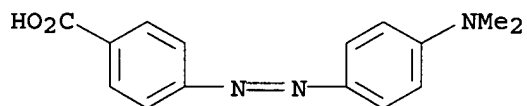
RN 2321-07-5 HCAPLUS

CN Spiro[isobenzofuran-1(3H),9'-[9H]xanthen]-3-one, 3',6'-dihydroxy- (9CI)
(CA INDEX NAME)



RN 6268-49-1 HCAPLUS

CN Benzoic acid, 4-[[4-(dimethylamino)phenyl]azo]- (9CI) (CA INDEX NAME)



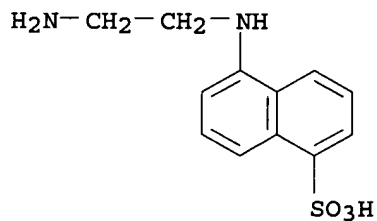
RN 7440-53-1 HCAPLUS

CN Europium (8CI, 9CI) (CA INDEX NAME)

Eu

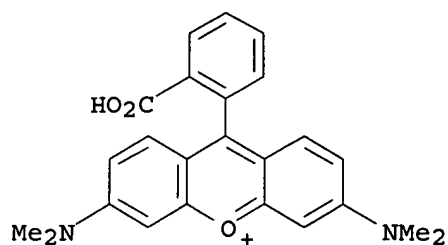
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CN 1-Naphthalenesulfonic acid, 5-[(2-aminoethyl)amino]- (9CI) (CA INDEX NAME)



RN 70281-37-7 HCAPLUS

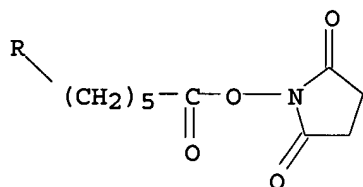
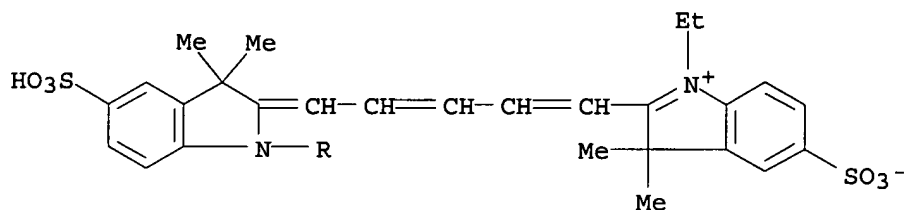
CN Xanthylum, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)-, chloride (9CI)
(CA INDEX NAME)



● Cl⁻

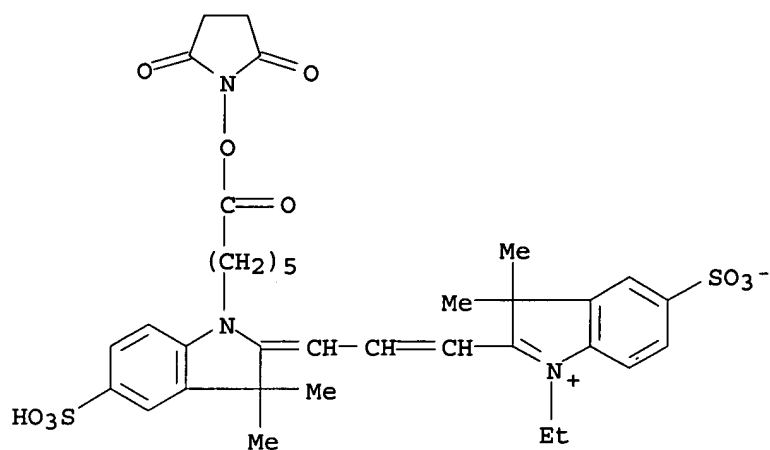
RN 146368-14-1 HCAPLUS

CN 3H-Indolium, 2-[5-[1-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1,3-pentadienyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)



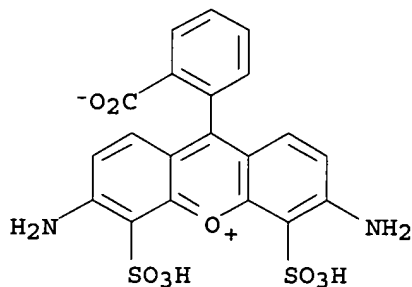
RN 146368-16-3 HCAPLUS

CN 3H-Indolium, 2-[3-[1-[6-[(2,5-dioxo-1-pyrrolidinyl)oxy]-6-oxohexyl]-1,3-dihydro-3,3-dimethyl-5-sulfo-2H-indol-2-ylidene]-1-propenyl]-1-ethyl-3,3-dimethyl-5-sulfo-, inner salt (9CI) (CA INDEX NAME)



RN 247144-99-6 HCAPLUS

CN Xanthylum, 3,6-diamino-9-[2,4(or 2,5)-dicarboxyphenyl]-4,5-disulfo-, inner salt, trilithium salt (9CI) (CA INDEX NAME)

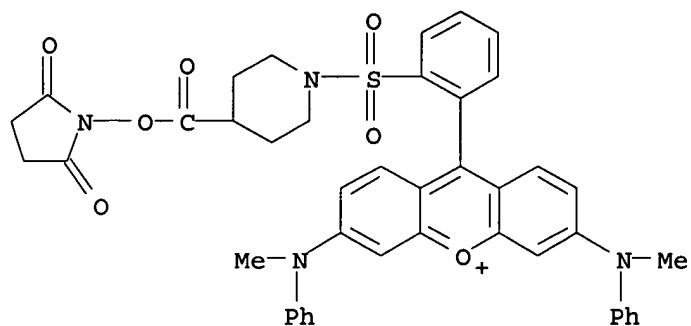


D1-CO₂H

●3 Li

RN 304014-12-8 HCAPLUS

CN Xanthylum, 9-[2-[[4-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-1-piperidinyl]sulfonyl]phenyl]-3,6-bis(methylphenylamino)-, chloride (9CI) (CA INDEX NAME)



● Cl⁻

IT 264902-77-4P, 3: PN: DE19849073 SEQID: 3 unclaimed DNA
 366520-85-6P
 RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (nucleotide sequence; **isolation** of functionally active
 γ -**secretase** presenilin 1 complex and
 fluorescence assay for γ -**secretase** activity
 and inhibitors)
 RN 264902-77-4 HCAPLUS
 CN 3: PN: DE19849073 SEQID: 3 unclaimed DNA (9CI) (CA INDEX NAME)

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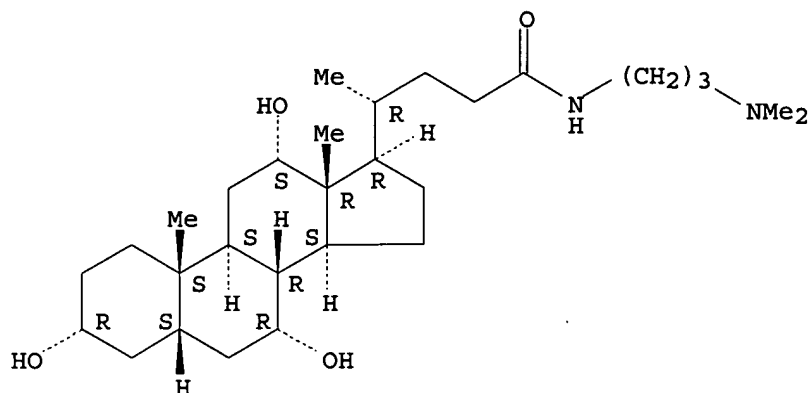
RN 366520-85-6 HCAPLUS
 CN DNA (synthetic human amyloid precursor protein isoform C-83-specifying)
 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 76555-98-1
 RL: NUU (Other use, unclassified); USES (Uses)
 (solubilizer; **isolation** of functionally active
 γ -**secretase** presenilin 1 complex and
 fluorescence assay for γ -**secretase** activity
 and inhibitors)

RN 76555-98-1 HCAPLUS
 CN Cholan-24-amide, N-[3-(dimethylamino)propyl]-3,7,12-trihydroxy-,
 (3α,5β,7α,12α) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 366522-29-4 366801-12-9 366801-14-1

RL: PRP (Properties)

(unclaimed protein sequence; **isolation** of functionally active
 γ -**secretase** presenilin 1 complex and
 fluorescence assay for γ -**secretase** activity
 and inhibitors)

RN 366522-29-4 HCAPLUS

CN 7: PN: WO0175435 SEQID: 8 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 366801-12-9 HCAPLUS

CN 9: PN: WO0175435 SEQID: 10 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 366801-14-1 HCAPLUS

CN 10: PN: WO0175435 SEQID: 11 unclaimed protein (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 199164-91-5 366488-00-8 366488-01-9

RL: PRP (Properties)

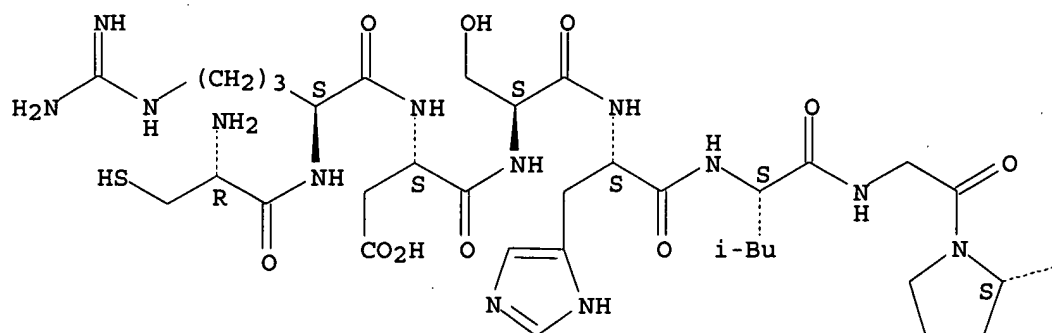
(unclaimed sequence; **isolation** of functionally active
 γ -**secretase** presenilin 1 complex and
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 and inhibitors)

RN 199164-91-5 HCAPLUS

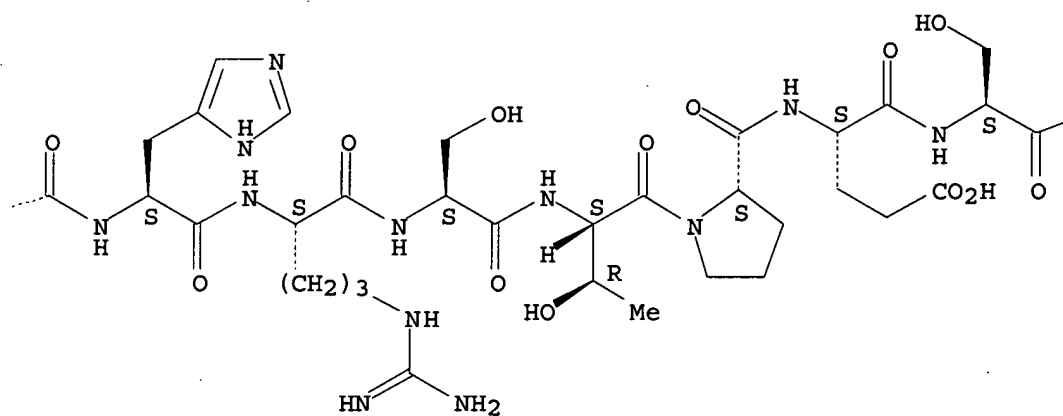
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 leucylglycyl-L-prolyl-L-histidyl-L-arginyl-L-seryl-L-threonyl-L-prolyl-L-
 α -glutamyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

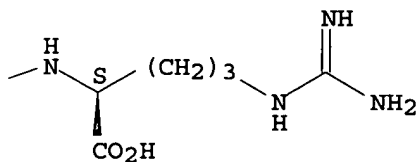
PAGE 1-A



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PAGE 1-C

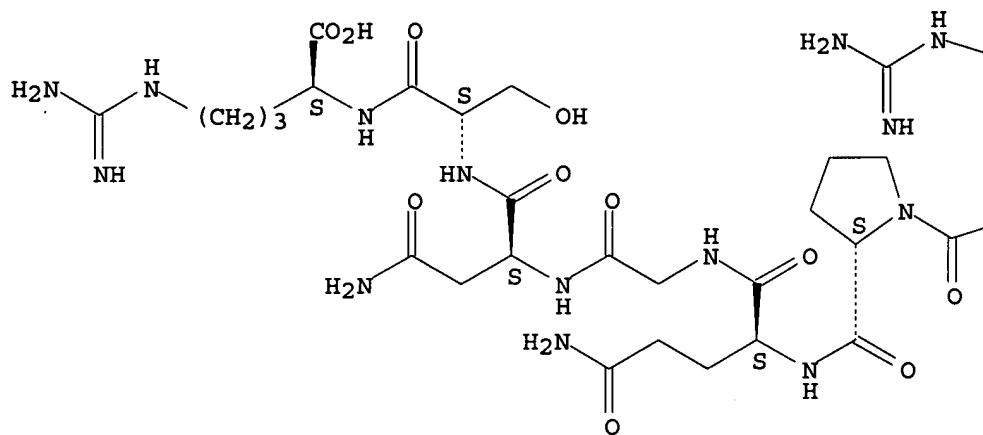


RN 366488-00-8 HCAPLUS

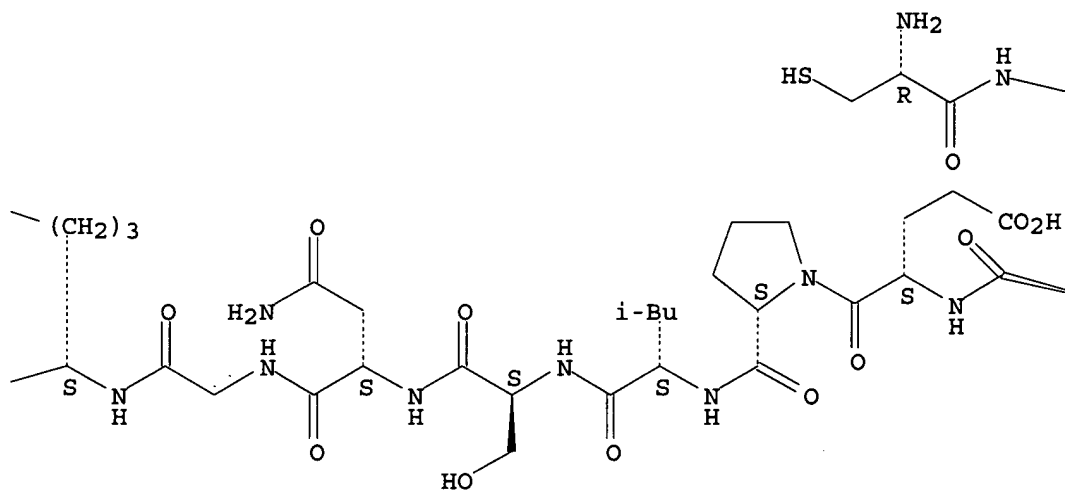
CN L-Arginine, L-cysteinylglycyl-L-histidyl-L-prolyl-L- α -glutamyl-L-prolyl-L-leucyl-L-seryl-L-asparaginylglycyl-L-arginyl-L-prolyl-L-glutaminylglycyl-L-asparaginyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

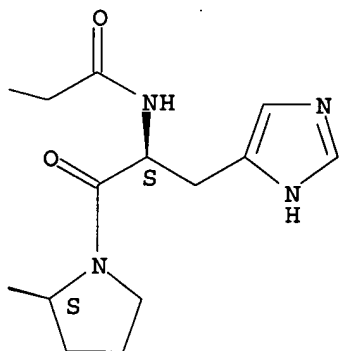
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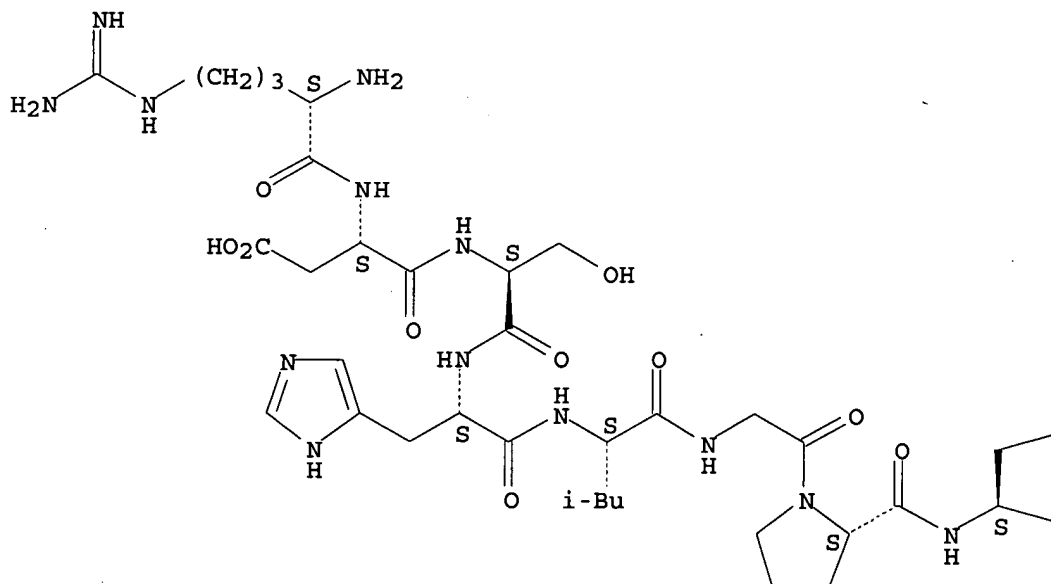


RN 366488-01-9 HCAPLUS

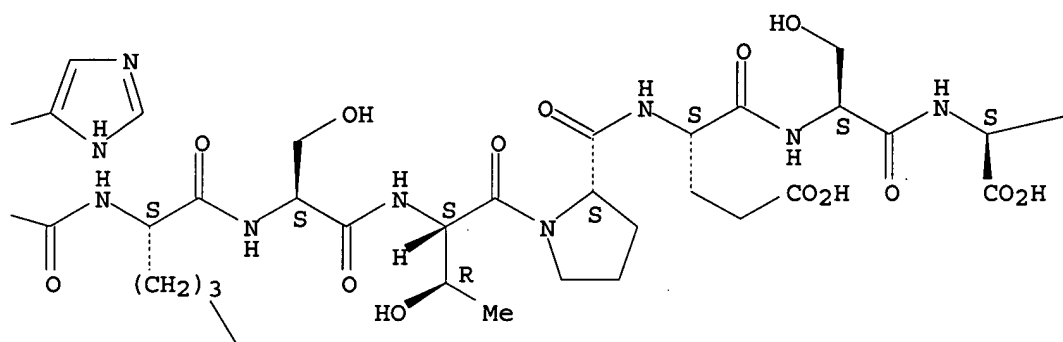
CN L-Arginine, L-arginyl-L- α -aspartyl-L-seryl-L-histidyl-L-leucylglycyl-L-prolyl-L-histidyl-L-arginyl-L-seryl-L-threonyl-L-prolyl-L- α -glutamyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

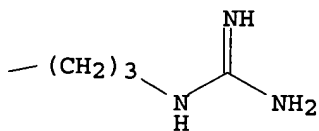
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